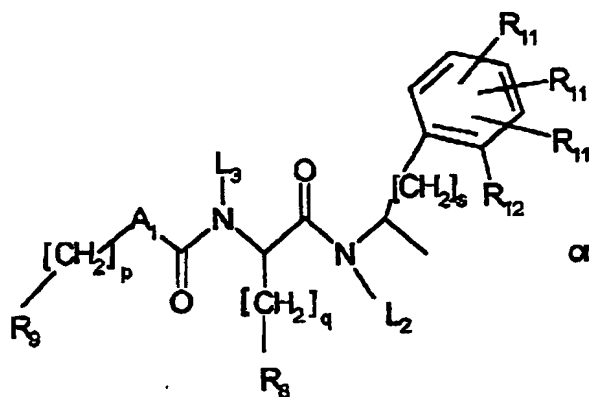




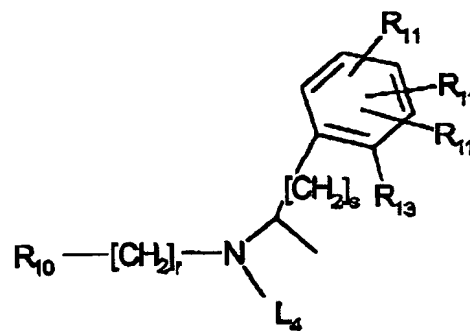
- 45 -

wherein  $R_7$  is either a group of formula (2) of formula (3):



Formula (2)

or



Formula (3)

wherein:

$L_2$ ,  $L_3$  and  $L_4$  are each independently hydrogen or methyl;

$R_8$  is amino, guanadino, imidazolo, any of which can be mono or di-N-substituted with  $C_{1-4}$ alkyl;

$A_1$  is oxygen or a direct bond;

$R_9$  is a  $C_{5-8}$  membered mono-carbocyclic ring, a  $C_{6-10}$  membered bi-carbocyclic ring,  $C_{8-12}$  membered tri-carbocyclic ring,  $C_{5-7}$ alkyl or aryl, any of which can be optionally mono, bi or tri substituted by  $C_{1-4}$  alkyl;

$R_{10}$  is  $C_{1-6}$ alkyl or a  $C_{3-8}$ mono-carbocyclic ring;

$R_{11}$  is hydrogen, halo,  $C_{1-4}$ alkyl, or  $C_{1-4}$ alkoxy;

$R_{12}$  is hydrogen or methyl or ethyl or  $R_{12}$  together with  $L_2$  forms a  $C_{5-7}$  nitrogen-containing heterocyclic ring;

$R_{13}$  is hydrogen or methyl ethyl or  $R_{13}$  together with  $L_4$  forms a  $C_{5-7}$  nitrogen-containing heterocyclic ring;

$n$  is 0, 1 or 2;

$p$  is 0, 1 or 2;

$q$  is an integer from 1 to 6

$r$  is 0, 1 or 2;

$s$  is 0, 1 or 2;

- 46 -

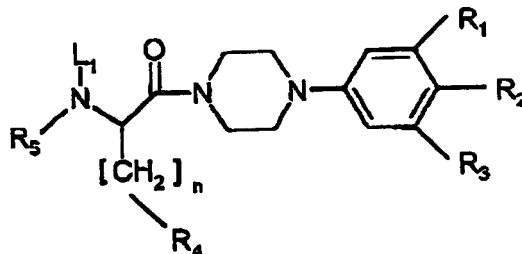
provided that when  $R_6$  is aryl, heteroaryl, heterocyclyl, amino $C_{3-6}$ alkyl,  $N$ -( $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl or  $NN$ -(di $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl then  $R_5$  is other than  $R_6CH_2-$ ; and when  $R_1$  to  $R_3$  are each hydrogen,  $L_1$  is hydrogen,  $n$  is 1,  $R_4$  is phenyl,  $R_5$  is  $R_6C(O)-$ , then  $R_6$  cannot be 2-methyl-4-amino-butyl, and excluding (S)-4-chloro-N-[1-(1H-indol-3-ylmethyl)-2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-N-methyl-benzamide; or a pharmaceutically acceptable salt, prodrug or solvate thereof.

2. A compound according to claim 1 wherein  $R_5$  is hydrogen.
3. A compound according to claim 2 wherein  $R_1$  is hydrogen;  $R_2$  is nitro;  $R_3$  is hydrogen;  $n$  is 1;  $R_4$  is indole,  $N$ -( $C_{1-4}$  alkyl)indole, cyclohexyl or phenyl any of which can be optionally substituted on ring carbon atoms with up to three substituents each independently selected from halo,  $C_{1-4}$ alkyl, or  $C_{1-4}$ alkoxy,  $L_1$  is hydrogen and  $R_5$  is hydrogen.
4. A compound according to claim 1 wherein  $R_5$  is  $R_6C(O)-$ ;  $R_6$  is aryl, heteroaryl, heterocyclyl, amino $C_{3-6}$ alkyl,  $N$ -( $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl, or  $NN$ -(di $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl, wherein the aryl, heteroaryl or heterocyclyl rings can be optionally substituted on ring carbon atoms with up to three substituents each independently selected from nitro, halo,  $C_{1-4}$ alkyl, or  $C_{1-4}$ alkoxy.
5. A compound according to claim 4 wherein  $R_1$  is hydrogen;  $R_2$  is nitro;  $R_3$  is hydrogen;  $n$  is 1;  $L_1$  is hydrogen; and  $R_6$  is aryl or heteroaryl wherein the aryl or heteroaryl can be optionally substituted on ring carbon atoms with up to three substituents each independently selected from nitro, halo,  $C_{1-4}$ alkyl, or  $C_{1-4}$ alkoxy.
6. A compound according to claim 1 wherein  $R_6$  is  $R_7$ .

- 47 -

7. A compound according to claim 6 wherein  $R_7$  is of Formula (2)
8. A compound according to claim 7 wherein  $R_1$  is hydrogen;  $R_2$  is nitro;  $R_3$  is hydrogen;  $n$  is 1;  $L_1$  is hydrogen;  $L_2$  is hydrogen or methyl;  $q$  is an integer between 2 and 4;  $R_8$  is amino;  $s$  is 1 and  $L_3$  is hydrogen or methyl.
9. A compound according to claim 6 wherein  $R_7$  is of Formula (3).
10. A compound according to claim 9 wherein  $R_1$  is hydrogen;  $R_2$  is nitro;  $R_3$  is hydrogen;  $n$  is 1;  $s$  is 1 and  $L_1$  is hydrogen,
11. A compound selected from the following:  
4,5-dimethoxy-2-nitrobenzoyl-Phe(4-Cl)-piperazine-4-nitrophenyl;  
4,5-dimethoxy-2-nitrobenzoyl-NMe-Trp-piperazine-4-nitrophenyl;  
4,5-dimethoxy-2-nitrobenzoyl-(D)(N<sup>m</sup>-Me)Trp-piperazine-4-nitrophenyl;  
Z-(D)(NMe)Dab-(NMe)(D)Phe-(D)Trp-piperazine-4-nitrophenyl;  
Z-NMe(D)Lys-NMe(D)Phe-(D)Phe(4-Cl)-piperazine-4-nitrophenyl;  
cyclohexyl-CO-(D)Lys-(D)NMe-Phe-Cha-piperazine-4-nitrophenyl;  
cyclohexyl-(D)Lys-(D)(NMe)Phe-(D)Phe(4-Cl)-piperazine-4-nitrophenyl;  
cyclohexyl-CH<sub>2</sub>-(D,L)NMe-Phe{CH<sub>2</sub>NH}(D)Trp-piperazine-4-nitrophenyl; and  
cyclohexyl-(D)Lys-(D)(NMe)Phe-(D)hPhe-piperazine-4-nitrophenyl;  
or a pharmaceutically acceptable salt, prodrug or solvate thereof.
12. A pharmaceutical composition which comprises a compound according to claims 1 to 11 and a pharmaceutically acceptable carrier.
13. The use in the treatment of a warm-blooded animal, by therapy, a compound of formula (1), or a pharmaceutically acceptable salt, prodrug or solvate thereof.

14. The use of a compound of Formula (4) in the manufacture of a medicament for the treatment of cancer in a warm-blooded animal.



formula (4)

wherein :

$L_1$  is hydrogen or methyl;

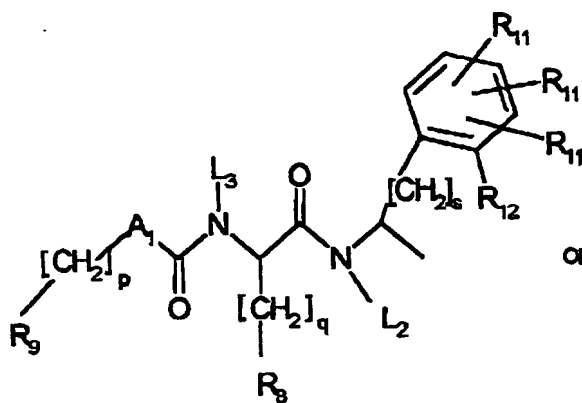
$R_1$  and  $R_2$  and  $R_3$  are each independently hydrogen, halo, nitro, cyano, carbamoyl, N-( $C_{1-4}$ alkyl)carbamoyl, NN-(di $C_{1-4}$ alkyl)carbamoyl or  $C_{1-4}$ alkoxycarbonyl;

$R_4$  is indole, N-( $C_{1-4}$  alkyl) indole,  $C_{3-7}$ carbocyclic ring or aryl, any of which can be optionally substituted on ring carbon atoms with up to three substituents each independently selected from halo,  $C_{1-4}$ alkyl, or  $C_{1-4}$ alkoxy;

$R_5$  is hydrogen,  $C_{1-4}$ alkyl,  $R_6CH_2-$  or  $R_6C(O)-$ ;

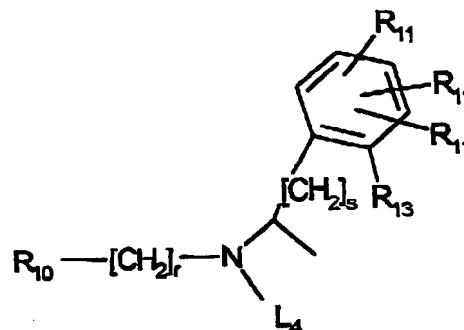
$R_6$  is aryl, heteroaryl, heterocyclyl, amino $C_{3-6}$ alkyl, N-( $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl, NN-(di $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl, or  $R_7$ ; wherein the aryl, heteroaryl or heterocyclyl rings may be optionally substituted with up to three substituents independently selected from nitro,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, halo, ( $C_{1-4}$ alkyl)sulfanyl,  $C_{1-4}$ alkoxycarbonyl, N-( $C_{1-4}$  alkyl)carbamoyl, NN-(di $C_{1-4}$  alkyl)carbamoyl, N-( $C_{1-4}$  alkyl)amino or NN-(di $C_{1-4}$  alkyl)amino;

wherein  $R_7$  is either a group of formula (5) of formula (6):



Formula (5)

or



Formula (6)

wherein:

$L_2$ ,  $L_3$  and  $L_4$  are each independently hydrogen or methyl;

$R_8$  is amino, guanadino, imidazolo, any of which can be mono or di-N-substituted with C<sub>1-4</sub>alkyl;

$A_1$  is oxygen or a direct bond;

$R_9$  is a C<sub>5-8</sub> membered mono-carbocyclic ring, a C<sub>6-10</sub> membered bi-carbocyclic ring, C<sub>8-12</sub> membered tri-carbocyclic ring, C<sub>5-7</sub>alkyl or aryl, any of which can be optionally mono, bi or tri substituted by C<sub>1-4</sub> alkyl;

$R_{10}$  is C<sub>1-6</sub>alkyl or a C<sub>3-8</sub>mono-carbocyclic ring;

$R_{11}$  is hydrogen, halo, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>alkoxy;

$R_{12}$  is hydrogen or methyl or ethyl or  $R_{12}$  together with  $L_2$  forms a C<sub>5-7</sub> nitrogen-containing heterocyclic ring;

$R_{13}$  is hydrogen or methyl ethyl or  $R_{13}$  together with  $L_4$  forms a C<sub>5-7</sub> nitrogen-containing heterocyclic ring;

$n$  is 0, 1 or 2;

$p$  is 0, 1 or 2;

$q$  is an integer from 1 to 6

$r$  is 0, 1 or 2;

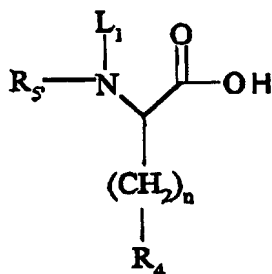
$s$  is 0, 1 or 2;

- 50 -

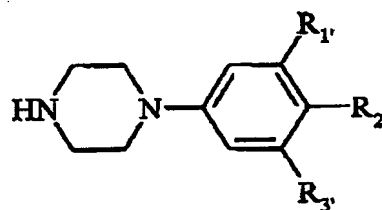
provided that when  $R_6$  is aryl, heteroaryl, heterocyclyl, amino $C_{3-6}$ alkyl,

$N$ -( $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl or  $NN$ -(di $C_{1-4}$ alkyl)amino $C_{3-6}$ alkyl then  $R_5$  is other than  $R_6CH_2-$ ; or a pharmaceutically acceptable salt, prodrug or solvate thereof.

15. A method of treating cancers which comprises administering to a warm-blooded animal an effective amount of a compound of formula (4).
16. A pharmaceutical composition comprising a compound of formula (4), or a pharmaceutically acceptable salt, prodrug or solvate thereof, in admixture with a pharmaceutically-acceptable diluent or carrier for the treatment of cancer in a warm-blooded animal.
17. A process for preparing a compound of the formula (1) or a pharmaceutically acceptable salt, prodrug or solvate thereof which process comprises:
  - a) reacting a carboxylic acid of Formula (8) or a reactive derivative thereof with a piperazine of formula (9)



Formula (8)

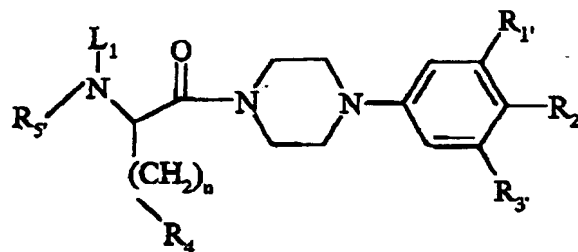


Formula (9)

wherein  $L_1$ ,  $n$ ,  $R_4$ ,  $R_1$ - $R_3$  and  $R_5$  are as herein above defined.

To form a compound of Formula (7)

- 51 -



Formula (7)

- b) removing any protecting groups,
- c) optionally forming a pharmaceutically acceptable salt, prodrug or solvate.

AMENDED SHEET  
IPEA/EP